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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/531,145	05/19/2005	Ke Liu	234872	7496

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EXAMINER	
CHEN, SHIN LIN	
ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/531,145	LIU ET AL.	
	Examiner	Art Unit	
	Shin-Lin Chen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) *15-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4-12-05 & 12-21-06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election with traverse of group I, claims 1-14, in the reply filed on 4-19-07 is acknowledged. The traversal is on the ground(s) that there is no serious burden on the Examiner if no restriction and the Office does not provide evidence that either '556 patent or Liu discloses the use of retroviral vector which does not comprises an exogenously introduced gene that enables phenotypic selection but comprises a viral envelope that efficiently transduces CD8+ T lymphocytes. Applicants argue that the main invention should include claims 1-16 because claims 2-26 are either directly or indirectly dependent on claim 1, similarly, claims 17-32 should be examined together. . This is not found persuasive because of the reasons of record. The retrovirus expressing human IL-2 a taught by '556 and Liu does not comprise an exogenously introduced gene affecting phenotypic selection, for example a neo gene or a HSV-TK gene, and the retrovirus inherently comprise a viral envelope that efficiently transduces CD8+ T-lymphocytes. Further, since no special technical feature has been contributed by the instant invention over the prior art, therefore, inventions I and II do not relate to a single general inventive concept. A method of preparing autologous T-lymphocytes and a method of treating a patient with said autologous T lymphocytes have different design and mode of operation, and they differ in objectives, method steps and criteria of success. There would be serious burden on Examiner to search inventions I-IV.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 15-32 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 4-19-07.

Applicants' preliminary amendment filed 4-12-05 has been entered. Claims 11-16 and 27-32 have been amended. Claims 1-32 are pending and claims 1-14 are under consideration.

Specification

3. Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of **50 to 150 words**. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

The abstract submitted on 4-12-05 exceeds 150 words. Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "wherein the antigen is amino acids 209-217 of gp100 with a methionine substitution at position 210 (209-2M peptide) in claim 4 is vague and renders the claim indefinite. There could be different gp100 amino acid sequences, and amino acids 209-217

could represent different amino acid sequences. It is unclear what amino acids 209-217 of gp100 refer to. It is unclear what the reference amino acid sequence is for amino acids 209-217.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 1 and 14 are rejected under 35 U.S.C. 102(e) as being anticipated by Lupton et al., 1999 (US Patent No. 5,874,556, IDS).

Claims 1 and 14 are directed to a method of preparing autologous T-lymphocytes for reintroduction into a patient having a cancer comprising obtaining PBMCs from a patient immunized with an antigen of the cancer, stimulating the PBMCs with the antigen of the cancer in vitro, and transducing the PBMCs with a retroviral vector comprising a human IL-2 coding sequence under the control of a retroviral promoter, does not comprise an exogenously introduced gene that enables phenotypic selection and comprises a viral envelope that efficiently transduces CD8+ T-lymphocytes, and a composition comprising T lymphocytes produced by said method, wherein 75% or more of the T lymphocytes are CD8+.

Lupton teaches that "IL-2, for example, is a potent mitogen for cytotoxic T lymphocytes..., and the combination of antigen and IL-2 cause proliferation of primary CD8+ T

cells in vitro." (e.g. column 1, lines 62-65), "cytotoxic T cells specific to a particular type of tumor can be isolated and administered to a patient having a tumor, with the effect that the CTLs ameliorate the tumor.", and "T cells with apparent tumor specificity can be isolated from human tumors. Such human tumor infiltrating lymphocytes (TILs) have been expanded in vitro and used to treat cancer patients." (e.g. column 2, lines 7-19). Lupton further teaches introduction of a retroviral vector expressing stimulatory factor, such as IL-2, into an activated lymphocyte, such as CD8+ CTL, wherein expression of the IL-2 protein in lymphocyte can reduce dependency of the lymphocyte on T helper cells for proliferation (e.g. column 43, 44). The retroviral vector as taught by Lupton does not comprise an exogenously introduced gene affecting phenotypic selection, for example a neo gene or a HSV-TK gene, and the retrovirus inherently comprise a viral envelope that efficiently transduces CD8+ T-lymphocytes. It would be inherent that 75% or more of the T lymphocytes are CD8+ because Lupton teaches introduction of a retroviral vector expressing IL-2 into an activated lymphocyte CD8+ CTL. Thus, claims 1 and 14 are anticipated by Lupton.

8. Claims 1-4 and 14 are rejected under 35 U.S.C. 102(a) as being anticipated by Liu et al., 2001 (The Journal of Immunology, Vol. 167, p. 6356-6365, IDS).

Claims 1-4 and 14 are directed to a method of preparing autologous T-lymphocytes for reintroduction into a patient having a cancer, such as melanoma, comprising obtaining PBMCs from a patient immunized with an antigen of the cancer, stimulating the PBMCs with the antigen of the cancer in vitro, such as 209-2M peptide, and transducing the PBMCs with a retroviral vector comprising a human IL-2 coding sequence under the control of a retroviral promoter, does

not comprise an exogenously introduced gene that enables phenotypic selection and comprises a viral envelope that efficiently transduces CD8+ T-lymphocytes, and a composition comprising T lymphocytes produced by said method, wherein 75% or more of the T lymphocytes are CD8+.

Liu teaches retrovirally transducing melanoma-reactive human T lymphocytes with an exogenous human IL-2 gene and the transduced PBMC and cloned CD8+ T cells produced IL-2 and maintained viability after IL-2 withdrawal (e.g. abstract). The PBMCs are obtained after the eighth weekly s.c. injection with 209-2M peptide of the patient RP with metastatic melanoma (e.g. p. 6357, left column, 3rd paragraph). Liu teaches preparation of retroviral vector containing the IL-2 gene under the control of viral 5' long terminal repeat promoter (IL-2-IRES-YFP), and two packaging cell lines, Phoenix E and PY 67, are used for preparing retroviruses (p. 6357, left column, 1st and 2nd paragraphs). The retroviral vector as taught by Liu does not comprise an exogenously introduced gene affecting phenotypic selection, for example a neo gene or a HSV-TK gene, and the retrovirus inherently comprise a viral envelope that efficiently transduces CD8+ T-lymphocytes. It would be inherent that 75% or more of the T lymphocytes are CD8+ because Liu teaches introduction of a retroviral vector expressing IL-2 into an activated lymphocyte CD8+ CTL and clones CD8+ T cells producing IL-2. Thus, claims 1-4 and 14 are anticipated by Liu.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 1-3 and 5-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lupton et al., 1999 (US Patent No. 5,874,556, IDS) in view of Kwak et al., 2003 (US Patent No. 6,562,347 B1).

Claims 1-3 and 5-10 are directed to a method of preparing autologous T-lymphocytes for reintroduction into a patient having a cancer, such as melanoma, breast cancer, prostate cancer, and colon cancer, comprising obtaining PBMCs from a patient immunized with an antigen of the cancer, stimulating the PBMCs with the antigen of the cancer in vitro, and transducing the PBMCs with a retroviral vector comprising a human IL-2 coding sequence under the control of a retroviral promoter, does not comprise an exogenously introduced gene that enables phenotypic selection and comprises a viral envelope that efficiently transduces CD8+ T-lymphocytes. Claims 3, 6, 8 and 10 specify the antigen of the cancer is gp100, Her2/Neu, PSA and CEA, respectively.

Lupton teaches that "IL-2, for example, is a potent mitogen for cytotoxic T lymphocytes..., and the combination of antigen and IL-2 cause proliferation of primary CD8+ T

cells in vitro." (e.g. column 1, lines 62-65), "cytotoxic T cells specific to a particular type of tumor can be isolated and administered to a patient having a tumor, with the effect that the CTLs ameliorate the tumor.", and "T cells with apparent tumor specificity can be isolated from human tumors. Such human tumor infiltrating lymphocytes (TILs) have been expanded in vitro and used to treat cancer patients." (e.g. column 2, lines 7-19). Lupton further teaches introduction of a retroviral vector expressing stimulatory factor, such as IL-2, into an activated lymphocyte, such as CD8+ CTL, wherein expression of the IL-2 protein in lymphocyte can reduce dependency of the lymphocyte on T helper cells for proliferation (e.g. column 43, 44). The retroviral vector as taught by Lupton does not comprise an exogenously introduced gene affecting phenotypic selection, for example a neo gene or a HSV-TK gene, and the retrovirus inherently comprise a viral envelope that efficiently transduces CD8+ T-lymphocytes.

Lupton does not specifically teach using cancer antigen gp100, Her2/Neu, PSA or CEA.

Kwak teaches that gp100, carcino-embryonic antigen (CEA), HER2/neu and prostatic serum antigen (PSA) are known tumor antigens and using fusion polypeptide comprising a chemokine and a tumor antigen as either a protein or nucleic acid vaccine to elicit an immune response effective in treating cancer or effective in treating or preventing HIV infection (e.g. column 1, lines 15-22, column 4, lines 35-47). Kwak teaches analysis of PBMC proliferative response in vitro before and after immunization with tumor antigen fusion protein (e.g. column 33, lines 7-12).

It would have been obvious for one of ordinary skill in the art at the time of the invention to use gp100, Her2/Neu, PSA or CEA as antigen of cancer to immunize a patient or to stimulate PBMCs in vitro because Lupton teaches that T cells with apparent tumor specificity can be

isolated from human tumors and such human tumor infiltrating lymphocytes (TILs) have been expanded in vitro and used to treat cancer patients, and melanoma, breast cancer, prostate cancer and colon cancer are all well known human tumors and Kwak teaches that gp100, carcino-embryonic antigen (CEA), HER2/neu and prostatic serum antigen (PSA) are known tumor antigens.

One having ordinary skill in the art at the time the invention was made would have been motivated to do so in order to immunize a patient as taught by Kwak or to expand the TILs in vitro for treating a cancer patient as taught by Lupton with reasonable expectation of success.

12. Claims 1-3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lupton et al., 1999 (US Patent No. 5,874,556, IDS) in view of Wang et al., 2001 (Exp. Opin. Biol. Ther., Vol. 1, No. 2, p. 277-290, IDS).

Claims 1-3 are directed to a method of preparing autologous T-lymphocytes for reintroduction into a patient having a cancer, such as melanoma, comprising obtaining PBMCs from a patient immunized with an antigen of the cancer, stimulating the PBMCs with the antigen of the cancer in vitro, and transducing the PBMCs with a retroviral vector comprising a human IL-2 coding sequence under the control of a retroviral promoter, does not comprise an exogenously introduced gene that enables phenotypic selection and comprises a viral envelope that efficiently transduces CD8+ T-lymphocytes. Claim 3 specifies the antigen of the cancer is gp100.

Lupton teaches that "IL-2, for example, is a potent mitogen for cytotoxic T lymphocytes..., and the combination of antigen and IL-2 cause proliferation of primary CD8+ T

cells in vitro." (e.g. column 1, lines 62-65), "cytotoxic T cells specific to a particular type of tumor can be isolated and administered to a patient having a tumor, with the effect that the CTLs ameliorate the tumor.", and "T cells with apparent tumor specificity can be isolated from human tumors. Such human tumor infiltrating lymphocytes (TILs) have been expanded in vitro and used to treat cancer patients." (e.g. column 2, lines 7-19). Lupton further teaches introduction of a retroviral vector expressing stimulatory factor, such as IL-2, into an activated lymphocyte, such as CD8+ CTL, wherein expression of the IL-2 protein in lymphocyte can reduce dependency of the lymphocyte on T helper cells for proliferation (e.g. column 43, 44). The retroviral vector as taught by Lupton does not comprise an exogenously introduced gene affecting phenotypic selection, for example a neo gene or a HSV-TK gene, and the retrovirus inherently comprise a viral envelope that efficiently transduces CD8+ T-lymphocytes.

Lupton does not specifically teach using cancer antigen gp100.

Wang teaches that "using IL-2, stable human T-cell lines specifically recognizing autologous tumor cells could be expanded in vitro from excised tumor specimens" and "IL-2 was then used to expand in vitro Lymphokine-activated Killer (LAK) cells from peripheral blood monocytes (PBMC) and tumor-infiltrating lymphocytes (TIL) from tumor specimens for adoptive cell transfer" (e.g. p. 278, left column). Wang also teaches gp100/Pmel17 is a tumor antigen expressed by both melanoma cells and normal melanocytes and infecting dendritic cells (DC) with viral constructs encoding tumor antigen to stimulate autologous human T-cells (e.g. p. 278, right column, p. 280, left column).

It would have been obvious for one of ordinary skill in the art at the time of the invention to use gp100 as antigen of cancer to immunize a patient or to stimulate PBMCs in vitro because

Lupton teaches that T cells with apparent tumor specificity can be isolated from human tumors and such human tumor infiltrating lymphocytes (TILs) have been expanded in vitro and used to treat cancer patients, and melanoma are all well known human tumors and Wang teaches that gp100/Pmel17 is a tumor antigen expressed by melanoma cells and using DC expressing tumor antigen to stimulate autologous human T-cells.

One having ordinary skill in the art at the time the invention was made would have been motivated to do so in order to expand the TILs in vitro for treating a cancer patient as taught by Lupton or to stimulate autologous human T-cells as taught by Wang with reasonable expectation of success.

13. Claims 1 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Lupton et al., 1999 (US Patent No. 5,874,556, IDS) or Liu et al., 2001 (The Journal of Immunology, Vol. 167, p. 6356-6365, IDS) each in view of Einerhand et al., 2001 (US Patent No. 6,312,957 B1).

Claims 1 and 11 are directed to a method of preparing autologous T-lymphocytes for reintroduction into a patient having a cancer comprising obtaining PBMCs from a patient immunized with an antigen of the cancer, stimulating the PBMCs with the antigen of the cancer in vitro, and transducing the PBMCs with a retroviral vector comprising a human IL-2 coding sequence under the control of a retroviral promoter, does not comprise an exogenously introduced gene that enables phenotypic selection and comprises a viral envelope that efficiently transduces CD8+ T-lymphocytes. Claim 11 specifies the viral envelope protein is Gibbon ape leukemia virus envelope (GALV).

The teachings of Lupton and Liu are as discussed above. Lupton or Liu does not teach using GALV envelope protein.

Einerhand teaches pseudotyping retroviruses with VSV envelope protein or GALV envelope proteins to target different and possible more abundantly present receptors on the cell membrane so as to improve the P-PHSC transduction by retroviral vectors in gene therapy (e.g. column 1, last paragraph).

It would have been obvious for one of ordinary skill in the art at the time of the invention to use GALV envelope protein in a retroviral vector because Einerhand teaches pseudotyping retroviruses with GALV envelope proteins can improve target cell transduction by retroviral vectors in gene therapy.

One having ordinary skill in the art at the time the invention was made would have been motivated to do so in order to target different and possible more abundantly present receptors on the cell membrane so as to improve target cell transduction by retroviral vectors in gene therapy as taught by Einerhand with reasonable expectation of success.

14. Claims 1, 12 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Lupton et al., 1999 (US Patent No. 5,874,556, IDS) or Liu et al., 2001 (The Journal of Immunology, Vol. 167, p. 6356-6365, IDS) each in view of Roifman, C. M., 2000 (Pediatric Research, Vol. 48, No. 1, p. 6-11).

Claims 1, 12 and 13 are directed to a method of preparing autologous T-lymphocytes for reintroduction into a patient having a cancer comprising obtaining PBMCs from a patient immunized with an antigen of the cancer, stimulating the PBMCs with the antigen of the cancer

in vitro, and transducing the PBMCs with a retroviral vector comprising a human IL-2 coding sequence under the control of a retroviral promoter, does not comprise an exogenously introduced gene that enables phenotypic selection and comprises a viral envelope that efficiently transduces CD8+ T-lymphocytes. Claims 12 and 13 specify the retroviral vector further comprises a human IL-2 receptor alpha-chain coding sequence operably linked to a promoter.

The teachings of Lupton and Liu are as discussed above. Lupton or Liu does not teach the retroviral vector further comprising a human IL-2 receptor alpha-chain coding sequence operably linked to a promoter.

Roifman teaches that absence of alpha chain of IL-2 receptor affects differentiation of thymocytes. The beta and gamma chains of the IL-2 receptor together can form an IL-2 receptor of low affinity, however, the presence of the high-affinity receptor upon activated peripheral T cells is believed to be necessary for optimal proliferation responses to IL-2 after stimulation of the T-cell antigen receptor (e.g. abstract).

It would have been obvious for one of ordinary skill in the art at the time of the invention to use human IL-2 receptor alpha-chain coding sequence under the control of a promoter in a retroviral vector because Roifman teaches that alpha-chain of IL-2 receptor is critical for the presence of the high-affinity IL-2 receptor and it is necessary for optimal proliferation responses to IL-2 after stimulation of the T-cell antigen receptor.

One having ordinary skill in the art at the time the invention was made would have been motivated to do so in order to have optimal proliferation responses to IL-2 after stimulation of the T-cell antigen receptor as taught by Roifman with reasonable expectation of success.

15. Claims 1, 12 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Lupton et al., 1999 (US Patent No. 5,874,556, IDS) or Liu et al., 2001 (The Journal of Immunology, Vol. 167, p. 6356-6365, IDS) each in view of Hattori et al., 1990 (The Journal of Immunology, Vol. 144, No. 10, p. 3809-3815).

Claims 1, 12 and 13 are directed to a method of preparing autologous T-lymphocytes for reintroduction into a patient having a cancer comprising obtaining PBMCs from a patient immunized with an antigen of the cancer, stimulating the PBMCs with the antigen of the cancer in vitro, and transducing the PBMCs with a retroviral vector comprising a human IL-2 coding sequence under the control of a retroviral promoter, does not comprise an exogenously introduced gene that enables phenotypic selection and comprises a viral envelope that efficiently transduces CD8+ T-lymphocytes. Claims 12 and 13 specify the retroviral vector further comprises a human IL-2 receptor alpha-chain coding sequence operably linked to a promoter.

The teachings of Lupton and Liu are as discussed above. Lupton or Liu does not teach the retroviral vector further comprising a human IL-2 receptor alpha-chain coding sequence operably linked to a promoter.

Hattori teaches that lymphocytes from the human IL-2Ralpha chain transgenic mice constitutively express high affinity binding sites for human IL-2, consisting of transgenic human IL-2R alpha and endogenous murine IL-2beta, and easily proliferate in vitro in response to human IL-2 protein (e.g. abstract).

It would have been obvious for one of ordinary skill in the art at the time of the invention to use human IL-2 receptor alpha-chain coding sequence under the control of a promoter in a retroviral vector because Hattori teaches that lymphocytes from the human IL-2Ralpha chain

transgenic mice constitutively express high affinity binding sites for human IL-2 and easily proliferate in vitro in response to human IL-2 protein.

One having ordinary skill in the art at the time the invention was made would have been motivated to do so in order to have lymphocytes constitutively express high affinity binding sites for human IL-2 and easily proliferate in vitro in response to human IL-2 protein as taught by Hattori with reasonable expectation of success.

16. Claims 1, 12 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Lupton et al., 1999 (US Patent No. 5,874,556, IDS) or Liu et al., 2001 (The Journal of Immunology, Vol. 167, p. 6356-6365, IDS) each in view of Asami et al., 1996 (European Journal of Haematology, Vol. 57, p. 278-285).

Claims 1, 12 and 13 are directed to a method of preparing autologous T-lymphocytes for reintroduction into a patient having a cancer comprising obtaining PBMCs from a patient immunized with an antigen of the cancer, stimulating the PBMCs with the antigen of the cancer in vitro, and transducing the PBMCs with a retroviral vector comprising a human IL-2 coding sequence under the control of a retroviral promoter, does not comprise an exogenously introduced gene that enables phenotypic selection and comprises a viral envelope that efficiently transduces CD8+ T-lymphocytes. Claims 12 and 13 specify the retroviral vector further comprises a human IL-2 receptor alpha-chain coding sequence operably linked to a promoter.

The teachings of Lupton and Liu are as discussed above. Lupton or Liu does not teach the retroviral vector further comprising a human IL-2 receptor alpha-chain coding sequence operably linked to a promoter.

Asami teaches preparation of a retroviral vector containing the human IL-2 receptor alpha chain gene (TAC) as a reporter under the control of 5' LTR and neomycin phosphotransferase gene (neo) as a selectable marker under the control of an internal promoter and the use of said retroviral vector to determine the effectiveness of the vector for expression of the reporter gene in the packaging cell line GP+E86 (e.g. abstract).

It would have been obvious for one of ordinary skill in the art at the time of the invention to use human IL-2 receptor alpha-chain coding sequence under the control of a promoter in a retroviral vector because either Lipton or Liu and Asami teaches retroviral vectors and Asami teaches using a retroviral vector containing the human IL-2 receptor alpha chain gene (TAC) as a reporter under the control of 5' LTR to determine the effectiveness of the vector for expression of the reporter gene in the packaging cell line GP+E86.

One having ordinary skill in the art at the time the invention was made would have been motivated to do so in order to determine the effectiveness of the vector for expression of the reporter gene in the packaging cell line GP+E86 as taught by Asami with reasonable expectation of success.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (571) 272-0726. The examiner can normally be reached on Monday to Friday from 9:30 am to 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for this group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Shin-Lin Chen, Ph.D.

SHIN-LIN CHEN
PRIMARY EXAMINER